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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 26 MAR 2004


WIPO PCT

Applicant's or agent's file reference 11783-6/PAR	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/CA 03/00542	International filing date (day/month/year) 11.04.2003	Priority date (day/month/year) 12.04.2002
International Patent Classification (IPC) or both national classification and IPC G01N33/68		
Applicant O'DOWD, Brian, F. et al.		

- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 4 sheets, including this cover sheet.  
  
☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).  
  
 These annexes consist of a total of sheets.

- This report contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand  20.10.2003	Date of completion of this report  25.03.2004
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer  Moreno de Vega, C  Telephone No. +49 89 2399-7486



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. **PCT/CA 03/00542**

**I. Basis of the report**

1. With regard to the elements of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, Pages**

1-83 as originally filed

**Claims, Numbers**

1-123 as originally filed

**Drawings, Sheets**

1/5-5/5 as originally filed

**Sequence listing part of the description, pages:**

1-36, filed with the letter of 25.07.2003,

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.  
☐ filed together with the international application in computer readable form.  
☒ furnished subsequently to this Authority in written form.  
☒ furnished subsequently to this Authority in computer readable form.  
☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

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5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-123
	No: Claims	
Inventive step (IS)	Yes: Claims	1-123
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-123
	No: Claims	

2. Citations and explanations

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/CA03/00542

**Re Item V**

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement.**

Reference is made to the following documents:

D1: WO 99 05177 A (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA) 4 February 1999 (1999-02-04).

1. Claims 1-123 are considered to be novel. The known prior art does not disclose the screening methods and cells of the present invention comprising transfecting a cell with at least one nucleotide sequence encoding a protein comprising a transmembrane protein containing at least one nuclear localisation sequence (NLS) and a detectable moiety and permitting the expression of the encoded protein in the cell, contacting with a candidate compound and determining the distribution of the expressed protein in the cell relative to the distribution in a control cell.
2. Document D1 is considered to be the most relevant prior art with respect to the present invention. D1 provides recombinant nucleic acids encoding N-terminally altered alpha4 subunits of G-proteins, and methods for using such mutants for the screening of GPCR modulators, using downstream signalling such as calcium mobilization. The technical problem to be solved by the present invention is the provision of assays for testing novel compounds interacting with transmembrane proteins. The solution of the present invention is based on the finding that when a nucleated eukaryotic cell is transfected with a nucleotide sequence which encodes a GPCR or any other transmembrane protein containing an incorporated NLS, and the cell is permitted to express the nucleotide sequence, the expressed transmembrane protein travels first to the cell membrane and then to the cell nucleus, and that this transfer can be modulated by treating the transfected cell with a compound which interacts with the transmembrane protein. This solution was not suggested in the known prior art. Thus, claims 1-123 are considered to be inventive.

Present claims 1-123 meet therefore the requirements of Articles 33(2) and 33(3) PCT.